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CAUSE, EPIDEMIOLOGY, MODE OF TRANSMISSION AND MANAGEMENT OF COVID-19

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ABSTRACT

Corona virus is a pandemic disease according to WHO (World health organisation). COVID-19 is caused by acute respiratory syndrome coronaviruse2 (SARAS-CoV-2). Initially, COVID-19 was started in Wuhan, a central china in December, 2019. The CFR (case fatility rate) depend upon the availibity of health care, age and health problem with in the population. On 12 January 2020, the World Health Organization temporarily named the new virus as 2019 novel corona virus (2019-nCoV). The sporadic outbreaks of new types of CoVs remind us that CoVs are severe threat to affect the global public health. According to WHO, 87,137 cases was confirmed across worldwide since the beginning of the epidemic. Out of these, 2977 (3.42%) have been fatal. About 92% (79,968) of the confirmed cases were recorded in China, where almost all the deaths were also recorded (2,873, 96.5%) It is highly likely that new CoVID outbreaks are unavoidable in the future due to changes of the climate, ecology and increased interactions of human with animals. Thus, there is an urgent need to develop effective therapies and vaccines against COVID-19. At present, there is no vaccine or antiviral treatment for human corona virus, so that identifying the drug treatment options as soon as possible is critical for the response to the 2019-nCoV outbreak. There are general methods, which include broad-spectrum antiviral drugs and the redevelopment of new specific drugs based on the genome and biophysical understanding of individual corona viruses, are used to discover the pontential antiviral treatment of human pathogen corona virus. Antiviral drugs includes Lopinavir, Ritonavir, Nucleoside analogues, Neuraminidase inhibitors, Remdesivir, RNA synthesis inhibitors (such as TDF, 3TC), anti-inflammatory drug, could be the drug treatment options for 2019-nCoV. Therefore, the efficacy and safety of these drugs for 2019- nCoV still need to be further confirmed by clinical experiments.

KEYWORDS: COVID-19, CFR, 3 TC, TDF, SARAS-CoV-2.

INTRODUCTION:

Corona virus (COVID-19) is a infectious disease which is caused by severe acute respiratory syndrome.[1] Itis quickly spreading from its origin in Wuhan City of Hubei Province of China to the rest of the world.[2] The symptom of corona virus includes fever, cough, shortness of breath, muscle pain, sputum production, diarrhea and sore throat.[3] Till 24/03/2020 around 1,675,11cases of coronavirus disease 2019 (COVID-19) and 6606 deaths have been reported in the world. India has reported 551 cases and 10 deaths have been reported till date.

Initially, the new virus was called 2019-nCoV. After that, the task of experts of the International Committee on Taxonomy of Viruses (ICTV) termed it the SARS-CoV-2 virus as it is similar to the one that caused the SARS outbreak (SARS-CoVs). This new virus seems to be very contagious and has spread quickly to all over the world. The CoVs have become the major pathogens of emerging respiratory disease outbreaks. This viruses can cross species barriers and can cause, in humans, illness ranging from the common cold to more severe diseases such as MERS and SARS. Interestingly, these latter viruses have probably originated from bats and then moving into other mammalian hosts. The dynamics of SARS-Cov-2 are currently unknown, but there is speculation that it also has an animal origin. The potential for these viruses to grow to become a pandemic disease according WHO. On February 28, 2020, the effects of the epidemic caused by the new COVID-19 has developed as the situation is quickly evolved. World Health organizations coordinate information flows and issues directives and guidelines to reduce the impact of the threat. At the same time, scientists and information about the transmission mechanisms, the clinical spectrum of disease, new diagnostics, and prevention and therapeutic strategies are rapidly developing.

Similarly, the therapeutic strategies to deal with the infection are only supportive, and prevention aimed at reducing transmission in the community is our best weapon. Aggressive isolation measures in China have lead to a progressive reduction of cases in the last few days. Since, knowledge about this virus is rapidly evolving, readers are urged to update themselves regularly.

Cause:

Coronaviruses are nonsegmented, positive-sense single-stranded RNA viruses ranging from 60 nm to 140 nm in diameter with spike like projections on its surface giving it a crown like appearance under the electron microscope. The virion has a nucleocapsid which is composed of genomic RNA and phosphorylated nucleocapsid (N) protein, which is covered inside phospholipid bilayers and covered by two different types of spike proteins: the spike glycoprotein trimmer (S) that can be found in all CoVs. The membrane (M) protein (a type III transmembrane glycoprotein) and the envelope (E) protein are located among the S proteins in the virus envelope. CoVs were given their name based on the characteristic crown-like appearance. The structure of CoV virion is shown in Figure 1.

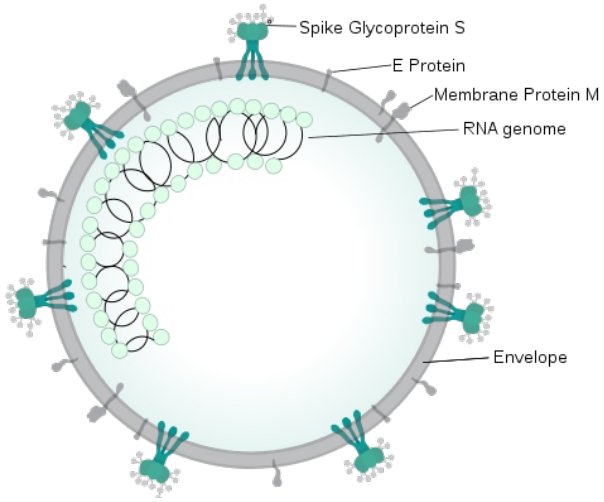

Fig. 1: Schematic representation of COVID-19 with spike like projection[4]

The coronavirus subfamily is divided into four genera, the α, β, γ, and δ coronaviruses. The β-coronavirus can be further classified into four viral lineages, namely lineage A-D. There are nearly 30 recognized CoVs that infect humans, mammals, fowl, and other animals. Human CoV infections are caused by α- and β-CoVs. CoVs are common human pathogens, and 30% to 60% of the Chinese population is positive for anti-CoV antibodies. The viral infections are generally associated with upper respiratory tract infections, of which the signs and symptoms commonly include fever, headache, and cough; some patients may have lower respiratory tract infections. In contrast, SARS-CoV and MERS-CoV infections may remain asymptomatic in the early stage until severe pneumonia, dyspnea, renal insufficiency, and even death.

Histopathological observations of pulmonary lesions in SARS cases not only show nonspecific inflammatory responses such as edema and inflammatory cell infiltration. Pathologically, inflammation includes degeneration (necrosis), infiltration, and hyperplasia. Thus, SARS-CoV infection can cause pathological changes, degeneration, infiltration, and hyperplasia. Damage to the pulmonary interstitial arteriolar walls indicates that inflammatory response plays an important role throughout the course of disease in spites of the pathogenic effect of CoVs.

Although the pathologies of SARS and MERS are not yet fully understood, viral and host factors play a key role in SARS-CoV and MERSCoV infections. During virus infection, host factors produce an immune response against the virus. However, it should be noted that immunopathogenesis is associated with an immune response out of control, which may result in pulmonary tissue damage, functional impairment, and reduced lung capacity. Chemotactic factors are essential to the immune responses against the virus infections, given their regulatory effect on dilations and positions of leukocytes in the host lungs. Therefore, spectral changes in chemotactic factors may lead to severely maladjusted immune responses. Immune insufficiency or misdirection may increase viral replication and cause tissue damages. In contrast, overactive immune responses may induce immune pathological conditions.

Hence, the four corona viruses namely HKU1, NL63, 229E and OC43 have been in circulation in humans, and generally cause mild respiratory disease.[5] The first such instance was in 2002–2003 when a new coronavirus of the β genera and with origin in bats crossed over to humans via the intermediary host of palm civet cats in the Guangdong province of China. This virus, designated as severe acute respiratory syndrome corona virus affected 8422 people mostly in China and Hong Kong and caused 916 deaths (mortality rate 11%) before being contained.[6] Almost a decade later in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV), also of bat origin, emerged in Saudi Arabia with dromedary camels as the intermediate host and affected 2494 people and caused 858 deaths (fatality rate 34%).[7]

Epidemiology:

In December 2019, adults in Wuhan, capital city of Hubei province and a major transportation hub of China started presenting to local hospitals with severe pneumonia of unknown cause. Many of the initial cases had a common exposure to the Huanan wholesale seafood market that also traded live animals. The surveillance system was activated and respiratory samples of patients were sent to reference labs for etiologic investigations. On December 31st 2019, China notified the outbreak to the World Health Organization and on 1st January the Huanan sea food market was closed. 7 January 2020, the virus was identified as a novel coronavirus by the WHO as 2019-nCoV. On 22 January 2020, 6 patients were died and total of 314 confirmed cases have been reported.On 13, 16, and 21 January, respectively, Thailand, Japan, and Korea were confirmed the detection of a human infection with 2019-nCoV from China. The number of cases started increasing exponentially, some of which did not have exposure to the live animal market, suggestive of the fact that human-to-human transmission was occurring.[8] By 23rd January, the 11 million population of Wuhan was placed under lock down with restrictions of entry and exit from the region. Soon this lock down was extended to other cities of Hubei province. Cases of COVID-19 in countries outside China were reported in those with no history of travel to China suggesting that local human-to-human transmission was occurring in these countries[9]. Cases continued to increase exponentially and modelling studies reported an epidemic doubling time of 1.8 d. In fact on the 12th of February, China changed its definition of confirmed cases to include patients with negative molecular tests but with clinical, radiologic and epidemiologic features of COVID-19 leading to an increase in cases by 15,000 in a single day.

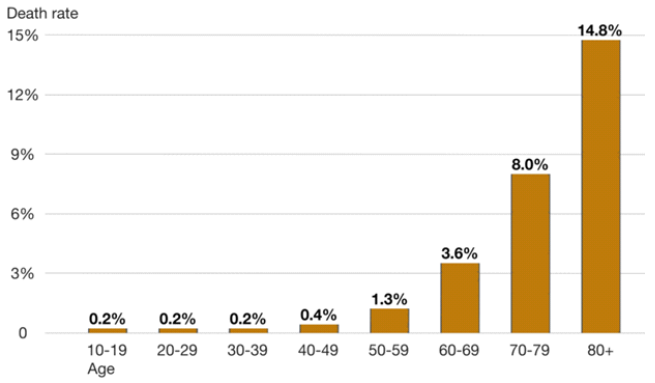

Fig. 2: Schematic representation of case fatality rate by age group in china till date 11/03/2020

As of 05/03/2020 96,000 cases worldwide (80,000 in China) and 87 other countries and 1 international conveyance (696, in the cruise ship Diamond Princess parked off the coast of Japan) have been reported. It is important to note that while the number of new cases has reduced in China lately, they have increased exponentially in other countries including South Korea, Italy and Iran. Of those infected, 20% are in critical condition, 25% have recovered, and 3310 (3013 in China and 297 in other countries) have died . India, which had reported only 3 cases till 2/3/2020, has also seen a sudden spurt in cases. By 5/3/2020, 29 cases had been reported; mostly in Delhi, Jaipur and Agra in Italian tourists and their contacts.

A total of 15,404 samples from 14514 individual have been tested for SARAS-CoV2 as on 20/03/2020 a total of 236 cases have been confirmed positive among suspected case and contacts as per ICMR.

Meanwhile, 69 years old Italian tourist who had recoverd from the novel corona virus died at private hospital in jaipur after massive cardiac arrest. As per ministery, Delhi has reported 17 positive cases while, uttar pardesh has recorded 28 cases, Karanatka has 15 corona virus patient, Rajasthan has also reprted 17 cases while Tamil Nadu, uttarakhand has been 17 cases reported. In Himachal Pardesh on 20/03/2020 have been confirmed its first two cases of corona virus from kangra have been reported. On 23 march,2020 italy death toll from corona virus outbreak rise from 602 to 6,077. A total of 274,783 cases people have been confirmed cases and 17,234 died in all over the world and 103,736 cases has been recovered.

Mode of transmission:

COVID02019 Infection is transmitted through large droplets during coughing and sneezing by symptomatic patients but can also occur from asymptomatic people. The novel coronavirus would spread to other geographic locations-including other countries-via direct human-to-human transmission.[9] Studies have shown higher viral loads in the nasal cavity as compared to the throat with viral difference between symptomatic and asymptomatic people . Patients can be infectious for as long as the symptoms last and even on clinical recovery. Some people may act as super spreaders; a UK citizen who attended a conference in Singapore infected11 other people while staying in a resort in the French Alps and upon return to the UK . These infected droplets can spread 1–2 m and deposit on surfaces. The virus can remain viable on surfaces for days in favourable atmospheric conditions but are destroyed in less than a minute by common disinfectants like sodium hypochlorite, hydrogen peroxide etc.[10] Infection is acquired either by inhalation of these droplets or touching surfaces contaminated by them and then touching the nose, mouth and eyes .[11]

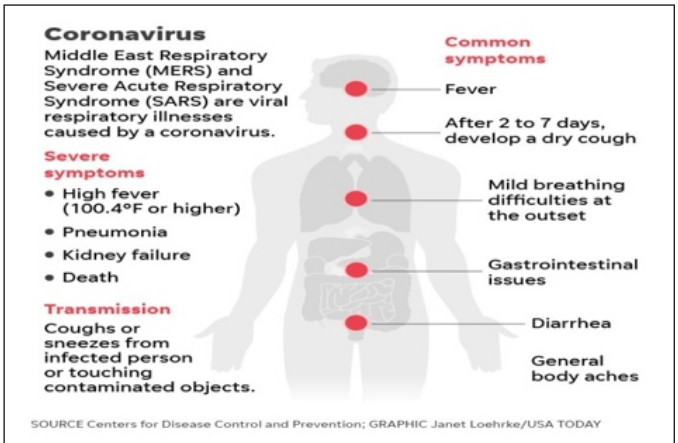

Fig. 3: Schematic representation of transmission of COVID-19

The virus is also present in the stool and contamination of the water supply and subsequent transmission via oral route is also hypothesized. [12] As per current information, transplacental transmission from pregnant women to their fetus has not been described [13]. However, neonatal disease due to post natal transmission is described. The incubation period varies from 2 to 14 days. Studies have identified angiotensin receptor 2 (ACE2) as the receptor through which the virus enters the respiratory mucosa. The basic case reproduction rate (BCR) is estimated to range from 2 to 6.47 in various modelling studies [11]. In comparison, the BCR of SARS was 2 and 1.3 for pandemic flu H1N1 2009.[14]

Management of COVID-19:

At present, there is no vaccine or antiviral treatment for human and animal coronavirus (COV). Because of its key role in the virus cell receptor interaction, the surface structure of spike glycoprotein(s) is particularly important for the development of antiviral. Treatment of such severe influenza still presents multiple challenges. There are several general methods that could be used to discover a potential antiviral treatment for the human pathogen coronavirus.

The first one is used to test broad-spectrum antiviral drugs by using standard assays, which have been used to treat other viral infections .[15] These methods can measure the effects of these drugs on the viral production and plaque formation of living cells. Examples of drugs identified using this method include interferon I (IFN- α, β, κ, λ, etc.) and interferon II (interferonγ, etc.). These drugs have obvious advantages, known pharmacokinetic and pharmacodynamic properties, side effects and drug regimens. However, they have no specific anti coronavirus effect and may be related to serious adverse reactions.

The other method include redevelopment of new specific drugs based on the genome and biophysical understanding of individual coronaviruses.[16] Examples include siRNA molecules or inhibitors targeting specific viral enzymes involved in the viral replication cycle, mAb targeting host receptor, inhibitor of host cell

protease, inhibitor of host cell endocytosis virus, human derived or humanized mAb targeting S1 RBD and antiviral peptide targeting S2. Although most of these drugs have anti coronavirus activity in vitro and/ or in vivo, their pharmacokinetic and pharmacodynamic properties, as well as side effect characteristics, have yet to be evaluated in animal and human trials. In addition, development of these drugs can allow drugs to become clinically useful treatment options, but it usually takes several years to provide reliable treatment for patients. The main drawback of this approach is that although many of the identified drugs show anti-coronavirus activity in vitro, most of them are not clinically useful because they are associated with immunosuppression or have a value of half the EC50 of anti-coronavirus, which is significantly higher than the peak serum concentration (Cmax) that can be achieved at the treatment dose.

For the current new coronavirus, according to the WHO guidelines[17], IFN- alpha and lopinavir/ritonavir (400 mg/100 mg bid) are recommended as antiviral therapy. IFN- alpha is a broad spectrum antiviral drug, which can be used to treat HBV. Lopinavir is only one protease inhibitor that is used to treat HIV infectio. Lopinavir and/or lopinavir litonavir have anti coronavirus activity in vitro. In Severe Acute Respiratory Syndrome (SARS) treatment, Hong Kong scholars found that compared with ribavirin alone, patients treated with lopinavir/ ritonavir and ribavirin had lower risk of acute respiratory distress syndrome (ARDS) or death.[18]

Similarly, Remdesivir may be the best potential drug for the treatment of 2019-nCoV. Animal experiments showed that compared with the control group, Remdesivir can effectively reduce the virus titer of mice infected with Middle East Respiratory Syndrome (Mers)-CoV, improve the lung tissue damage, and its effect is better than that of the treatment group treated with Lopinavir/Ritonavir combined with interferon-β. [19] However, the efficacy and safety of Remdesivir in patients with 2019-nCoV infection were further confirmed by clinical research.[20]

Although, some other types of drugs have been found to be effective in vitro, such as fusion peptide (EK1) [21], arbidol[22], RNA synthesis inhibitors (such as TDF, 3TC) anti-inflammatory drugs (such as hormones and other molecules), etc. similarly, Chinese medicine, such as ShuFengJieDu Capsules and Lianhuaqingwen Capsules, has also played a role in the prevention and treatment of new respiratory infectious diseases such as influenza A (H1N1).[23,24] However, the efficacy and safety of these drugs in 2019-nCoVwere further confirmed by clinical experiments.

Prevention:

Since, at this time there are no approved treatments for this infection, prevention is crucial. Several properties of this virus make prevention difficult namely, nonspecific features of the disease, transmission from asymptomatic people, long incubation period, tropism for mucosal surfaces such as the conjunctiva, prolonged duration of the illness and transmission even after clinical recovery. Isolation of confirmed or suspected cases with mild illness at home is recommended. The ventilation at home should be good with sunlight to allow for destruction of virus. Patients should be asked to wear a simple surgical mask and practice cough hygiene. Care givers should be asked to wear a surgical mask when in the same room as patient and use hand hygiene every 15–20 min. The greatest risk in COVID-19 is transmission to healthcare workers. In the SARS outbreak of 2002, 21% of those affected were healthcare workers.[25] Till 24/03/2020 around 1,675,11cases of coronavirus disease 2019 (COVID-19) and 6606 deaths have been reported in the world. India has reported 500 cases and 10 deaths have been reported till date. The doctor who first warned about the virus has died too. It is important to protect healthcare workers to ensure continuity of care and to prevent transmission of infection to other patients. While COVID-19 transmits as a droplet pathogen and is placed in Category B of infectious agents (highly pathogenic H5N1 and SARS), by the China National Health Commission, infection control measures recommended are those for category A agents (cholera, plague). Patients should be placed in separate rooms. Negative pressure rooms are not generally needed. The rooms and surfaces and equipment should undergo regular decontamination preferably with sodium hypochlorite. Airborne transmission precautions should be taken during aerosol generating procedures such as intubation, suction and tracheotomies. All contacts including healthcare workers should be monitored for development of symptoms of COVID-19

At the community level, people should be asked to avoid crowded areas and postpone non-essential travel to places with ongoing transmission. They should be asked to practice cough hygiene by coughing in sleeve/tissue rather than hands and practice hand hygiene frequently every 15–20 min. Patients with respiratory symptoms should be asked to use surgical masks. The use of mask by healthy people in public places has not shown to protect against respiratory viral infections and is currently not recommended by WHO.[26]

CONCLUSION:

This new virus outbreak has challenged the economic, medical and public health infrastructure of China and other countries. Time alone will tell how the virus will impact our lives here in India. More so, future outbreaks of viruses and pathogens of zoonotic origin are likely to continue. Therefore, away from curbing this outbreak, efforts should be made to construct comprehensive measures to prevent future outbreaks of zoonotic origin. Although these studies are relevant to control the current public emergency, more high-quality research is needed to provide valid and reliable ways to manage this kind of public health emergency in both the short- and long-term.

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